DEVICE AND METHOD FOR SELECTING ELECTROPHORESIS BAND

PRIORITY INFORMATION

This application claims priority to Japanese Application Serial No. 279861/2000, filed September 14, 2000.

FIELD OF THE INVENTION

The present invention relates to a device and a method for selecting an electrophoresis band. More particularly, the present invention relates to a user interface for simply and accurately selecting a band of interest from bands established on an image data, on a display screen displaying the image data obtained by picking up an electrophoresis pattern of a sample.

BACKGROUND OF THE INVENTION

In biochemical experiments, samples containing molecules such as DNA with various lengths are sometimes separated by electrophoresis. By electrophoresis, molecules such as DNA or proteins migrate on a gel by the application of an electric field, thereby being separated and established as bands according to their molecular weights. A range where bands have migrated from the same initial migration point is defined as a lane.

Figure **19** is a schematic diagram of an electrophoresis device. Hereinafter, separation of DNA molecules will be described as an example. The electrophoresis device **1903** is provided with a negative (-) electrode **1904** and a positive (+) electrode **1905**, which are connected to a power source **1901** via a conductor **1902**. A sample is put into a sample

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inlet **1906** on the (-) electrode **1904** side, and a voltage is applied. As a result, negatively-charged DNA molecules are electrically pulled and thus migrate from the (-) electrode **1904** side toward the (+) electrode **1905** side. According to the difference of the molecular weights, the molecules are separated into a DNA molecule **1908** of a larger molecular weight, a DNA molecule **1909** of a middle molecular weight and a DNA molecule **1910** of a small molecular weight. The path where these DNA molecules have migrated is a lane **1915**. The states of the DNA molecules separated on the lane **1915** can be observed with a CCD camera or the like, and may be analyzed by image processing.

For image processing, the DNA molecules present on the lane **1915** are established as bands on an image of the post-migration DNA molecules. The bands can be established automatically by reading the brightness of pixels on the lane, integrating the brightness in the migration direction **1907** from the sample inlet **1906** and in the direction perpendicular to the migration direction **1907**, and detecting a peak position **1917** from a generated spectrum **1916**. Then, lines perpendicular to the migration direction **1907** are drawn on the lane **1915** at positions corresponding to the peak positions, thereby setting a band **1911** (the DNA molecule **1908**), a band **1913** (the DNA molecule **1909**) and a band **1914** (the DNA molecule **1910**).

When the lane **1915** is contaminated by dust **1919**, the

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dust **1919** will appear as a peak **1918** on the spectrum **1916**, and could be mistakenly detected as a band **1912**. In order to carry out the experiment, the setting of the error band **1912** must be cleared. For this purpose, the image processor is provided with a band selecting function. In general, in order to select a band, an operator inputs a band selecting command with a pointing unit such as a mouse looking at the bands displayed on the image display unit. When the band to be selected is too small or too narrow to be selected with the pointing unit, a predetermined range of the band displaying region is enlarged to ease the selection.

In order to select a band on the image with the pointing unit such as a mouse according to the band selecting function of a conventional image processor, the cursor of the pointing unit must accurately point the band of interest on the lane displayed on the image display unit. Furthermore, when the band of interest is very close to another band or is in the middle of a group of gathering bands, the band regions overlapping in the image makes it difficult or impossible to designate the band of interest with the pointing unit.

In view of such problems of an image processor for processing electrophoresis image data, the present invention has an objective of providing a device and method for simply and efficiently selecting and displaying a band present on a lane.

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SUMMARY OF THE INVENTION

In order to accomplish the above-described objective, the device of the present invention is provided with an image memory for storing electrophoresis image data, an image display input unit for performing input on a display screen displaying the image data, and a processor for selecting bands of the image data by inputting a selection region on a lane with a pointing unit and inputting a selection command to the image data on the display screen with a keyboard. Based on the input of the selection region of the lane and the selection command, the bands to be selected are determined and displayed in a selection candidate state distinctively from other bands on the screen of the image display input unit.

Instead of inputting the selection region and the selection instruction with the pointing unit alone, the pointing unit may be used together with a keyboard to select a band of interest in an easier and more accurate manner.

According to the present invention, a device for selecting an electrophoresis band of interest from a plurality of bands on an electrophoresis lane of a sample comprises: a display unit for displaying an image of the plurality of bands established on the lane; a region setting unit for setting a region on the lane on a screen of the display unit; a region altering unit for altering the size of the region; a selection candidate displaying unit for

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displaying bands within the region in a selection candidate state; and a band selecting unit for processing the bands in the selection candidate state to be in a selection state.

Display in the selection candidate state refers to a clear distinction of the selection candidates such as a display with a different color or a blinking display which is different from a usual display. The bands in the selection candidate state may be processed to be in a selection state (the bands may be selected for sure) with a band selecting unit, for example, by clicking a mouse button or by pressing an enter key of a keyboard.

Preferably, the region setting unit sets the region on the lane by setting an input cursor of a pointing unit on the lane at the center, and the region altering unit alters the size of the region in accordance with the press of a predetermined key of a keyboard.

Preferably, the device further comprises a band information displaying unit for displaying the number of bands in the selection candidate state relative to the region.

According to the present invention, a device for selecting an electrophoresis band of interest from a plurality of bands on an electrophoresis lane of a sample, comprises: a display unit for displaying an image of the plurality of bands established on the lane; a region setting unit for setting a region on the lane on a screen of the display unit; a selection candidate displaying unit for displaying one of the bands within the region, in a selection

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candidate state; a selection candidate display altering unit for altering the band in the selection candidate state to a band immediately before or after the former band along the lane; and a band selecting unit for processing the band in the selection candidate state to be in a selection state.

Preferably, the region setting unit sets the region on the lane based on a position of an input cursor of a pointing unit on the lane (e.g., where the position of the input cursor is set the center), the selection candidate displaying unit displays a band closest to the input cursor in the selection candidate state, and the selection candidate display altering unit alters the band to be displayed in the selection candidate state in accordance with the press of a predetermined key of a keyboard.

Preferably, the device further comprises a region altering unit for altering the size of the region in accordance with the press of a predetermined key of the keyboard.

The device of the invention may further comprise a band information displaying unit for displaying information of the bands displayed in the selection candidate state relative to the region.

The information of the bands in the selection candidate state may be, for example, relative positions of the bands within the established region.

According to the present invention, a method for selecting an electrophoresis band of interest from a

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plurality of bands on an electrophoresis lane of a sample, comprises the steps of: setting a region on the lane based on an input cursor of a pointing unit placed on the display of the lane having a plurality of bands; displaying bands within the region in a selection candidate state; altering the size of the region in accordance with an key input of a predetermined key of a keyboard, as well as altering states of bands that became included in the region as the result of the size alteration from a normal state to the selection candidate state and states of bands that fell out from the region as the result of the size alteration from the selection candidate state to the normal state; and displaying selected bands of the bands in the selection candidate state in a selection state in response to a selection input.

The selection command may be inputted by clicking a button of a mouse (the pointing unit) or by pressing an enter key of the keyboard. By this input of the selection command, bands in the selection candidate state is processed to be in a selection state (i.e., selected for sure).

According to the present invention, a method for selecting an electrophoresis band of interest from a plurality of bands on an electrophoresis lane of a sample, comprises the steps of: setting a region on the lane based on an input cursor of a pointing unit placed on the display of the lane having a plurality of bands; displaying a band within the region, which is closest to the input cursor, in a selection candidate state; altering the band in the selection

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candidate state to a band immediately before or after the former band along the lane in accordance with the press of a predetermined key of a keyboard; and processing the band in the selection candidate state to be in a selection state.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure **1** is a block diagram showing an exemplary structure of a band selecting device of the invention.

Figure **2** is a view showing examples of lanes and bands on an electrophoresis gel.

Figure **3** is a diagram showing switching of band selection modes in accordance with a keyboard input.

Figure **4** is a schematic view for illustrating a display of a selection candidate region.

Figure **5** is a schematic view for illustrating a selection candidate display and a band information display of bands within the selection candidate region under the all-band selection mode.

Figure **6** is a schematic view for illustrating a selection candidate display and a band information display of bands within the selection candidate region under the single-band selection mode.

Figure **7** is a flowchart showing a process under a normal mode.

Figure **8** is a flowchart for showing a general process under the all-band selection mode.

Figure **9** is a flowchart for showing the general process under the all-band selection mode.

Figure **10** is a flowchart for showing a general process under the single-band selection mode.

Figure **11** is a flowchart for showing the general process under the single-band selection mode.

Figure **12** is a flowchart showing an enlargement/reduction operation of a selection candidate region.

Figures **13A** and **13B** are schematic views showing an operation for reducing a size of a selection candidate region in a horizontal direction.

Figures **14A** and **14B** are schematic views showing an operation for enlarging a selection candidate region in a horizontal direction.

Figures **15A** and **15B** are schematic views showing an operation for reducing a size of a selection candidate region in a vertical direction.

Figures **16A** and **16B** are schematic views showing an operation for enlarging a selection candidate region in a vertical direction.

Figure **17** is a flowchart showing an operation of switching a band to be in a selection candidate state under the single-band selection mode.

Figure **18** is a diagram showing an exemplary structure of a data memory.

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Figure **19** is a schematic diagram for illustrating electrophoresis bands and lanes, and migration of DNA molecules.

DETAILED DESCRIPTION OF THE INVENTION

Hereinafter, embodiments of the present invention will be described with reference to the attached drawings.

Figure **1** is a block diagram showing an exemplary structure of a device of the invention for selecting an electrophoresis band. The band selecting device is provided with a central processing unit **101** for processing various operations, a program memory **102** for storing programs necessary for the operations by the central processing unit **101**, an image memory **103**, a data memory **104**, an interactive operation input unit **105** and a display unit **106** as a display screen.

The program memory **102** stores a selection candidate region displaying program **121**, a selection candidate region band determining program **122**, a selection candidate state operating program **123**, an information generating program **124** and an information displaying program **125**. The image memory **103** stores image data **131** obtained by picking up an image of the sample of interest. The data memory **104** stores lane data **141** which is information of the image data in an area determined as a lane, and band data **142** which is information of the image data of areas determined as bands. The lane

data **141** and the band data **142** store information of the lane locations and the band locations in a coordinates data style.

A band selection operation is carried out by a computer program. The present system can be implemented in a usual manner with a personal computer or a workstation. The program recorded on a storage medium such as a magnetic storage or a CD-ROM is installed in a hard disk and executed by the central processing unit **101**. Alternatively, the program may be downloaded from a network (e.g., online circuit or the Internet) into the hard disk.

Figure **18** shows an exemplary structure of the data memory. The data memory **104** stores number of lanes **N** as well as the lane data. The lane data **141** stores positional data of a lane and data of bands on the lanes. The relative positions of the lane on an image are stored in the lane data **141**. The positions of the bands relative to the lane are stored in band data **142** included in the data memory **104**. Thus, the data memory **104** and the image memory **103** are stored in separate spaces. The lane and the bands are displayed based on the lane data **141** and the band data **143** in the data memory **104**.

The selection candidate region displaying program **121** stored in the program memory **102** displays a selection candidate region on the display unit **106**, where the center position is determined by an input with the pointing unit **151** (e.g., a mouse) of the interactive operation input unit **105**. The selection candidate region band determining program **122**

reads out the lane data **141** and the band data **142** via the operation of the central processing unit **101** to determine the presence of bands within the selection candidate region. The selection candidate state operating program **123** processes the bands that are determined by the selection candidate region band determining program **122** to be in a selection candidate state. The information generating program **124** generates information of bands within the selection candidate region. The information displaying program **125** displays the information of the bands within the selection candidate region generated by the information generating program **124** on the display unit **106**.

Figure **2** is a view of lanes and bands on an electrophoresis gel. Molecules that have migrated from the starting point **201** as a result of electrophoresis are established as bands **202**. The range where the bands **202** have migrated from the single starting point **202** is set as a lane **203**.

Figure **3** is a diagram showing transition of band selection modes which are switched from one to another in accordance with an input with the keyboard **152** of the interactive operation input unit **105**. The band selecting device of the invention has two band selection modes, all-band selection mode for selecting all of the bands within the selected region of the lane and single-band selection mode for selecting a single band. A normal mode **301** where the selection and display of the bands are not carried out is

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switched to the all-band selection mode **302** by pressing a predetermined key (e.g., "5" key) on the keyboard. The all-band selection mode **302** is switched to the single-band selection mode **303** by pressing a predetermined key (e.g., "5" key) on the keyboard. The single-band selection mode **303** is switched to the all-band selection mode **302** by pressing a predetermined key (e.g., "5" key) on the keyboard. The all-band selection mode **302** and the single-band selection mode **303** can be returned to the normal mode **301** by pressing a predetermined key (e.g., "0" key) on the keyboard.

Figure **4** is a schematic view for illustrating a display of the selection candidate region **402** where the input cursor **401** of the pointing unit is set at the center. When the input cursor **401** of the pointing unit of the interactive operation input unit **105** is placed on the lane **403**, a selection candidate region **402** of a predetermined size is displayed for the lane **403** with the coordinates of the input cursor **401** being at the center. The size of the selection candidate region **402** may be altered as described below by using predetermined keys of the keyboard (e.g., arrow keys " , " , " and ").

Figure **5** is a schematic view for illustrating a selection candidate display and a band information display of the bands within the selection candidate region under the all-band selection mode. When coordinates are designated with an input cursor **501** of the pointing unit, a selection candidate region **502** is displayed on a lane **503** with the

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designated coordinates being at the center as described above.
Bands **504** and **505** outside the selection candidate region **502**
are represented by solid lines as usual display, whereas
bands **506, 507** and **508** within the selection candidate region
502 are represented by broken lines as a selection candidate
display. Instead of representing the bands within the
selection candidate region **502** by broken lines as in the
figure, they may alternatively be displayed by any other
style (e.g., different color or blinking display) as long as
they are distinct from other bands. When the input cursor
501 moves on the lane **503,** the position of the selection
candidate region **502** also moves on the lane **503,** according to
which the selection candidate bands also change.

Information such as the number of bands within the
selection candidate region **502** is displayed as selection
candidate region band information **509** in the vicinity of the
selection candidate region **502.** In the case of Figure **5,** the
selection candidate region band information **509** tells that
three bands are present in the selection candidate region **502.**
The size of the selection candidate region **502** may be altered
as described below by a keyboard operation. As the size of
the selection candidate region **502** is altered, the selection
candidate bands and selection candidate region band
information **509** also change.

Figure **6** is a schematic view for illustrating a
selection candidate display and a band information display of
the bands within the selection candidate region under the

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single-band selection mode. When coordinates are designated with an input cursor **601** of the pointing unit, a selection candidate region **602** is displayed on a lane **603** with the coordinates designated by the cursor **601** being at the center as described above. Bands **604** and **605** outside the selection candidate region **602** are represented by solid lines as usual display, whereas a band **608** which is the closest band to the input cursor **601** of the pointing unit within the selection candidate region **602** is represented by a broken line as a selection candidate display. Other bands **606** and **607** are represented by solid lines as a usual display although they are present within the selection candidate region. When the input cursor **601** moves on the lane **603**, the position of the selection candidate region **602** also moves on the lane **603**, according to which the selection candidate band also changes to a band closest to the input cursor.

Information such as the number of bands within the selection candidate region **602** is displayed as selection candidate region band information **609** in the vicinity of the selection candidate region **602**. In the case of Figure **6**, the selection candidate region band information **609** tells that total of three bands are present in the selection candidate region **602** and that one band is present above and one band is present under the selection candidate display band. The size of the selection candidate region **602** may be altered as described below by a keyboard operation. As the size of the

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selection candidate region **602** is altered, the selection candidate region band information **609** also changes.

Figure **7** is a flowchart showing a process under the normal mode. In step **701**, whether or not the "5" key of the keyboard is pressed is checked. If the "5" key is determined to be pressed, the process proceeds to Step **702** to switch to the all-band selection mode and ends. If the "5" key is determined to be unpressed, the process ends without any operation.

Figures **8** and **9** are flowcharts showing the whole process under the all-band selection mode. In Step **801**, whether or not the "5" key of the keyboard is pressed is checked. If the "5" key is determined to be pressed, the process proceeds to Step **802** to switch to the single-band selection mode and ends. If the "5" key is determined to be unpressed, the process proceeds to Step **803**. In Step **803**, whether or not the "0" key of the keyboard is pressed is checked. If the "0" key is determined to be pressed, the process proceeds to Step **804** to switch to the normal mode and ends. If the "0" key is determined to be unpressed, the process proceeds to Step **805**.

In Step **805,** the center coordinates of the selection candidate region are input with the pointing unit. Specifically, the input cursor of the pointing unit is moved to a desired position on a desired lane. In Step **806**, the selection candidate region is displayed where the coordinates input at Step **805** is set at the center. In Step **807,** whether

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an arrow key of the keyboard is pressed is checked. When the
arrow key is determined to be pressed, the process proceeds
to Step **808** to perform an enlargement/reduction operation **808**
for the selection candidate region. The
enlargement/reduction operation **808** will be described below
with reference to Figure **12**. In the subsequent Step **809**,
selection candidates determination and settings for the all-
band selection mode are performed.

In the following Step **810**, the bands set as the
selection candidates are displayed. In the next Step **811**,
information of the bands in the selection candidate region is
generated and displayed. In Step **812**, whether or not
clicking operation is performed with the pointing unit is
checked. If a click with the pointing unit is determined to
have taken place, the process proceeds to Step **813**. In Step
813, the bands within the selection candidate region are
displayed in a selection state.

Figures **10** and **11** are flowcharts showing the whole
process under the single-band selection mode. In Step **1001**,
whether or not the "5" key of the keyboard is pressed is
checked. If the "5" key is determined to be pressed, the
process proceeds to Step **1002** to switch to all-band selection
mode and ends. If the "5" key is determined to be unpressed,
the process proceeds to Step **1003**. In Step **1003**, whether or
not the "0" key of the keyboard is pressed is checked. If
the "0" key is determined to be pressed, the process proceeds
to Step **1004** to switch to the normal mode and ends. If the

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"0" key is determined to be unpressed, the process proceeds to Step **1005**.

In Step **1005**, the center coordinates of the selection candidate region are inputted with the pointing unit. Specifically, the input cursor of the pointing unit is moved to a desired position on a desired lane. In Step **1006**, the selection candidate region is displayed where the coordinates input at Step **1005** is set at the center. In Step **1007**, whether an arrow key of the keyboard is pressed is checked. When the arrow key is determined to be pressed, the process proceeds to Step **1008** to perform an enlargement/reduction operation **1008** for the selection candidate region. The enlargement/reduction operation **1008** will be described below with reference to Figure **12**. In the subsequent Step **1009**, selection candidates determination and settings for the single-band selection mode are performed.

In the following Step **1010**, whether or not the "8" or "2" key of the keyboard is pressed is checked. If the "8" or "2" key is determined to be pressed, the process proceeds to Step **1011** and switching operation **1011** takes place for the selection candidate band displayed under the single-band selection mode. Details of the switching operation **1011** for the selection candidate band will be described with reference to Figure **17**. In the following Step **1012**, the bands set as the selection candidates are displayed. In the next Step **1013**, information of the band in the selection candidate region is generated and displayed. In Step **1014**, whether or

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not a clicking operation by the pointing unit is performed is checked. If the clicking operation by the pointing unit is determined to have taken place, the process proceeds to Step **1015**. In Step **1015**, the bands within the selection candidate region are displayed in a selection state.

Figure **12** is a flowchart for showing the enlargement/reduction operation of the selection candidate region by a keyboard input under the all-band selection mode and the single-band selection mode. In Step **1201**, whether or not the " (left pointing arrow)" key is pressed is checked. If the " (left pointing arrow)" key is determined to be pressed, the operation proceeds to Step **1202** to reduce the size of the selection candidate region in horizontal direction and ends the operation. As shown in Figures **13A** and **13B**, when this operation is performed for the selection candidate region **1301**, the size of the region **1301** is reduced in the horizontal direction while the position of the cursor **1302** is set at the center, thereby setting a new selection candidate region **1311**.

If the " (left pointing arrow)" key is determined to be unpressed, the operation proceeds to Step **1203**. In Step **1203**, whether or not the " (right pointing arrow)" key is pressed is checked. If the " (right pointing arrow)" key is determined to be pressed, the operation proceeds to Step **1204** to enlarge the selection candidate region in horizontal direction and ends the operation. As shown in Figures **14A** and **14B**, when this operation is performed for the selection

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candidate region **1401**, the region **1401** is enlarged in the
horizontal direction while the position of the cursor **1402** is
set at the center, thereby setting a new selection candidate
region **1411**.

If the " (right pointing arrow)" key is determined to
be unpressed, the operation proceeds to Step **1205**. In Step
1205, whether or not the " (up pointing arrow)" key is
pressed is checked. If the " (up pointing arrow)" key is
determined to be pressed, the operation proceeds to Step **1206**
to reduce the size of the selection candidate region in
vertical direction and ends the operation. As shown in
Figures **15A** and **15B**, when this operation is performed for the
selection candidate region **1501**, the size of the region **1501**
is reduced in the vertical direction while the position of
the cursor **1502** is set at the center, thereby setting a new
selection candidate region **1511**.

If the " (up pointing arrow)" key is determined to be
unpressed, the operation proceeds to Step **1207**. In Step **1203**,
whether or not the " (down pointing arrow)" key is pressed
is checked. If the " (down pointing arrow)" key is
determined to be pressed, the operation proceeds to Step **1208**
to enlarge the selection candidate region in vertical
direction. As shown in Figures **16A** and **16B**, when this
operation is performed for the selection candidate region
1601, the region **1601** is enlarged in the vertical direction
while the position of the cursor **1602** is set at the center,
thereby setting a new selection candidate region **1611**.

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Figure **17** is a flowchart showing the switching operation of a selection candidate band by a keyboard input under the single-band selection mode. In Step **1701**, cursor coordinates are input with the pointing unit. In Step **1702**, the band closest to the cursor coordinates input in Step **1701** is processed to be in a selection candidate state. In Step **1703**, whether or not the "8" key of the keyboard is pressed is checked. If the "8" key is determined to be pressed, the operation proceeds to Step **1704**, where a band immediately before the band in the selection candidate state (with respect to the electrophoresis direction) is set to be in the selection candidate state, and end the operation. If the "8" key is determined to be unpressed in Step **1703**, the operation proceeds to Step **1705**. In Step **1705**, whether the "2" key of the keyboard is pressed is checked. If the "2" key is determined to be pressed, the operation proceeds to Step **1706** where the band immediately after the band in the selection candidate state (with respect to the electrophoresis direction) is set to be in the selection candidate state, and end the operation. If the "2" key is determined to be unpressed in Step **1705**, the operation is ended.

By employing the present invention, only the band of interest can be selected from a group of gathering bands so that the selected band may be processed (e.g., deleted). Although specific keys are assigned for particular operations in the above description, these keys are only examples for clearer understanding of the invention. The present

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invention is not limited to the specific examples described herein.

According to the present invention, by using the keyboard and the pointing unit of the interactive input unit, a band on a screen may be displayed in a selection state in a simple and efficient manner.